Figure 1 (A). Sequence alignment of predicted KUZ proteins from Drosophila (DKUZ, SEQ ID NO:2), mouse (MKUZ, SEQ ID NO:8) and Xenopus (XKUZ, SEQ ID NO:10). The full length amino acid sequence of MKUZ was deduced from the nucleotide sequence of two overlapping cDNA clones. Partial amino acid sequence of XKUZ was deduced from the nucleotide sequence of a PCR product that includes parts of the disintegrin and Cys-rich domains. The alignments were produced using Geneworks software (IntelliGenetics). Residues identical among two species are highlighted. Predicted functional domains are indicated. Amino acid sequences from which degenerate PCR primers were designed are indicated with arrows. Orthologs of *kuz* are also present in C. elegans (GenBank accession nos. D68061 and M79534), rat (Z48444), bovine (Z21961) and human (Z48579).

a2

At p.5, line 14, before the paragraph beginning "The subject domains...", please insert the following paragraph:

Ordinarily, the allelic variants, the conservative substitution variants and the members of the *kuz* family of proteins, will have an amino acid sequence having at least 75% amino acid sequence identity with one or more of the disclosed human full length, human secreted form, mouse and *Drosophila kuz* protein sequences, more preferably at least 80%, even more preferably at least 90%, and most preferably at least 95%. Identity or homology with respect to such sequences is defined herein as percentage of amino acid residues in the candidate sequence that are identical with the known peptides, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent homology, and not considering any conservative substitutions as part of the sequence identity. N-terminal, C-terminal or internal extensions, deletions, or insertions into the peptide sequence shall not be construed as affecting homology.

a3

Please replace the paragraph bridging p.26 and 27 with the following paragraph:

Xenopus *kuz* was cloned by PCR using degenerate primers (XK1) and (XK4) which correspond to Drosophila KUZ sequence HNFGSPHD (SEQ ID NO:2, residues 609-616) and GYCDVF (SEQ ID NO:2, residues 870-875), respectively. First strand cDNA from stage 18

a4

Xenopus embryos was used as template in a standard PCR reaction with an annealing temperature of 50°C. A PCR product of expected size was purified and used as template for another PCR reaction using a nested primer (XK3), corresponding to Drosophila KUZ sequence EECDCG (SEQ ID NO:2, residues 688-693), and XK4. The PCR product was subcloned into Bluescript and sequenced. Anti-sense RNA was used as a probe for whole mount *in situ* hybridization of Xenopus embryos according to standard procedures (Harland, R. (1991). Meth. Cell Biol. *36*, 685-695).

a4 cont

At page 41, line 42, please insert the following text:

(2) INFORMATION FOR SEQ ID NO:9:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 486 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: cDNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

```
TACAGCGACC AATGTAAGGA TGAATGTTGC TATGATGCCA ATCAGCCAGA AAACCTAAAG      60
TGCACATTAA AGCCTGGAAA ACAGTGCAGT CCCAGCCAGG GCCCTTGTTG CACCACTGGA     120
TGTACCTTCA AGCGAGCAGG TGAGAACTGT CGGGAGGAAT CTGACTGTGC CAAGATGGGA     180
ACTTGCAATG GCAACTCTGC TCAGTGTCCA CCATCCGAAC CAAGAGAGAA CCTGACTGAG     240
TGTAACAGGG CAACCCAAGT TTGCATCAAG GGGCAATGCT CAGGATCTAT CTGTGAGAGG     300
TATGACTTGG AAGAGTGCAC TTGCGGCAGT ACTGATGAAA AAGATGACAA AGAGCTGTGC     360
CACGTTTGCT GCATGGAGAA AATGATACCG CACACATGTG CTAGCACTGG TTCAGAAGTA     420
TGGAAAGCTT ACTTTAAAGG AAAGACTATT ACGTTACAAC CAGGATCACC TTGCAATGAA     480
TTTAAA                                                               486
```

(2) INFORMATION FOR SEQ ID NO:10:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 162 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

```
Tyr Ser Asp Gln Cys Lys Asp Glu Cys Cys Tyr Asp Ala Asn Gln Pro
1               5                  10                  15
Glu Asn Leu Lys Cys Thr Leu Lys Pro Gly Lys Gln Cys Ser Pro Ser
            20                  25                  30
Gln Gly Pro Cys Cys Thr Thr Gly Cys Thr Phe Lys Arg Ala Gly Glu
        35                  40                  45
Asn Cys Arg Glu Glu Ser Asp Cys Ala Lys Met Gly Thr Cys Asn Gly
    50                  55                  60
Asn Ser Ala Gln Cys Pro Pro Ser Glu Pro Arg Glu Asn Leu Thr Glu
65                  70                  75                  80
Cys Asn Arg Ala Thr Gln Val Cys Ile Lys Gly Gln Cys Ser Gly Ser
                85                  90                  95
Ile Cys Glu Arg Tyr Asp Leu Glu Glu Cys Thr Cys Gly Ser Thr Asp
            100                 105                 110
Glu Lys Asp Asp Lys Glu Leu Cys His Val Cys Cys Met Glu Lys Met
        115                 120                 125
Ile Pro His Thr Cys Ala Ser Thr Gly Ser Glu Val Trp Lys Ala Tyr
    130                 135                 140
Phe Lys Gly Lys Thr Ile Thr Leu Gln Pro Gly Ser Pro Cys Asn Glu
145                 150                 155                 160
```